Normal range of intraoperative three-dimensional derived right ventricular strain in coronary artery bypass surgery patients

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Abstract

Objectives: Data on intraoperative three-dimensional derived right ventricular free-wall strain (3D-RV FWS) is sparse. We sought to evaluate the normal range of intraoperative 3D-RV FWS in patients scheduled for coronary artery bypass graft (CABG) surgery and compare to conventional echocardiographic parameters. *Design:* Prospective observational study. *Setting:* Single university hospital. *Participants:* 150 patients with preserved left and right ventricular function and sinus rhythm, without significant heart valve disease or pulmonary hypertension undergoing isolated onpump CABG surgery, with an uneventful, complication-free intraoperative course. *Interventions:* 3D-RV FWS analysis and conventional echocardiographic assessment of right ventricular function were performed intraoperatively in anesthetized and ventilated patients using transesophageal echocardiography (TEE). All echocardiographic measurements were performed under stable hemodynamic conditions and predefined fluid management without any vasoactive support or pacing. *Measurements and Main Results:* We used TomTec 4D RV-Function 2.0 software for assessment of 3D-RV FWS and three-dimensional right ventricular ejection fraction (3D-RV EF). Philips QLAB 10.8 was used to evaluate tissue velocity of the tricuspid annulus (RV S´), tricuspid annular systolic excursion (TAPSE), and RV fractional area change (FAC). Assessment of 3D-RV FWS was feasible in 95% of patients. No included patient experienced a serious perioperative complication. In our group of patients, median values with interquartile range (IQR) for 3D-RV FWS and 3D-RV EF were - 25.2 (IQR -29.9 - -21.8) and 46.3% (IQR 41.0 - 50.1%), respectively. RV FAC, RV S´ and TAPSE accounted for 39.7% (IQR 34.5 - 44.4%), 14.8cm/s (IQR 11.8 - 19.0cm/s) and 22 mm (IQR 20-25mm). Normal range (2.5% to 97.5% percentile) for 3D-RV FWS was -37.1 to -12.8. There was no relevant correlation of 3D-RV FWS to postoperative outcome in this group of CABG patients. *Conclusion:* We present distribution values for intraoperative 3D-RV FWS and conventional parameters of RV function assessment in a healthy on-pump CABG patient population without serious perioperative complications. We observed no correlations of these parameters with any of the outcome parameters considered. Therefore, we consider these values to be intraoperative TEE-assessed *normal* values that can be expected in onpump CABG patients.

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Conflict of Interest

The authors declare there are no conflicts of interest.

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Ethics Approval Statement

The institutional review board of the medical faculty of the Technical University of Dresden, Germany, approved this prospective observational study.

Patient Consensus Statement

All patients were enrolled between January 2019 and April 2020 after written informed consent.

Objectives: Data on intraoperative three-dimensional derived right ventricular free-wall strain (3D-RV FWS) is sparse. We sought to evaluate the normal range of intraoperative 3D-RV FWS in patients scheduled for coronary artery bypass graft (CABG) surgery and compare to conventional echocardiographic parameters.

Design: Prospective observational study.

Setting: Single university hospital.

Participants: 150 patients with preserved left and right ventricular function and sinus rhythm, without significant heart valve disease or pulmonary hypertension undergoing isolated onpump CABG surgery, with an uneventful, complication-free intraoperative course.

Interventions: 3D-RV FWS analysis and conventional echocardiographic assessment of right ventricular function were performed intraoperatively in anesthetized and ventilated patients using transesophageal echocardiography (TEE). All echocardiographic measurements were performed under stable hemodynamic conditions and predefined fluid management without any vasoactive support or pacing.

Measurements and Main Results: We used TomTec 4D RV-Function 2.0 software for assessment of 3D-RV FWS and three-dimensional right ventricular ejection fraction (3D-RV EF). Philips QLAB 10.8 was used to evaluate tissue velocity of the tricuspid annulus (RV S'), tricuspid annular systolic excursion (TAPSE), and RV fractional area change (FAC). Assessment of 3D-RV FWS was feasible in 95% of patients. No included patient experienced a serious perioperative complication.

In our group of patients, median values with interquartile range (IQR) for 3D-RV FWS and 3D-RV EF were - 25.2 (IQR -29.9 - -21.8) and 46.3% (IQR 41.0 - 50.1%), respectively. RV FAC, RV S' and TAPSE accounted for 39.7% (IQR 34.5 - 44.4%), 14.8cm/s (IQR 11.8 - 19.0cm/s) and 22 mm (IQR 20-25mm). Normal range (2.5% to 97.5% percentile) for 3D-RV FWS was -37.1 to -12.8.

There was no relevant correlation of 3D-RV FWS to postoperative outcome in this group of CABG patients.

Conclusion: We present distribution values for intraoperative 3D-RV FWS and conventional parameters of RV function assessment in a healthy on-pump CABG patient population without serious perioperative complications. We observed no correlations of these parameters with any of the outcome parameters considered. Therefore, we consider these values to be intraoperative TEE-assessed *normal* values that can be expected in onpump CABG patients.

Key Words: three-dimensional echocardiography; strain analysis; right ventricle; free wall strain; cardiac surgery; reference values

Introduction

Right ventricular (RV) function strongly predicts outcome after cardiac surgery.[1, 2] Echocardiography remains a cornerstone in detecting perioperative RV dysfunction, but the complex geometry of the right ventricle makes echocardiographic assessment still challenging.[3, 4] Conventional echocardiographic parameters for RV function assessment have numerous limitations including incomplete imaging of the complex crescent-shaped right ventricle and angle dependency of Doppler and M-mode technique.[5] Strain analysis with speckle-tracking echocardiography (STE) becomes an advancing technique to measure myocardial function. Myocardial strain analysis is less dependent on loading conditions, does not rely on geometric assumptions, has a smaller interobserver variability, is largely angle-independent and is an independent predictor of RV function.[6-8] Therefore, strain analysis seems particularly suitable for the perioperative assessment of the right ventricle. Most data on RV strain analysis, however, comes from the evaluation of awake spontaneously breathing patients using transthoracic echocardiography (TTE).[5, 9] Intraoperative evaluation of RV strain in anesthetized and ventilated patients using transesophageal echocardiography (TEE) is feasible and supports perioperative decision making, but there is only limited data.[7, 10] In particular, this is true for three-dimensional derived right ventricular strain analysis.[11, 12] Regardless of the possible benefit of three-dimensional derived RV strain, this technique is quite novel and is not well described in the intraoperative period. Evaluation is challenging by the fact that there are no established normal or reference values for the intraoperative setting. Therefore, by the present study we aim to close this gap by providing intraoperative values for three-dimensional derived right ventricular free-wall strain (3D-RV FWS) that can be expected in onpump coronary artery bypass grafting (CABG) patients with a complication-free, unremarkable intraoperative course.

Methods

Study Population

The institutional review board of the medical faculty of the Technical University of Dresden, Germany, approved this prospective observational study. 150 adult patients were enrolled between January 2019 and April 2020 after written informed consent. All patients had preoperative sinus rhythm and preserved LV and RV function. We excluded patients with contraindications to TEE, redo cardiac surgery, more than mild valvular heart disease, pulmonary hypertension (mean pulmonary artery pressure >25 mmHg), or insufficient quality of echocardiographic assessment preventing the analysis of three-dimensional data sets.

Anesthesia Management

Following our institutional protocol, anesthesia was induced with fentanyl, propofol, and rocuronium and was maintained with sevoflurane and fentanyl. Lungs were ventilated mechanically with a tidal volume of 6 to 8 mL/kg with a positive end-expiratory pressure of [?] 5 mbar, maintaining normoxia and normocapnia. Patients were restricted to a maximum of 500 mL of balanced crystalloid infusion till intraoperative echocardiography. All echocardiographic measurements were performed without any influence of inotropic or vasopressor support and pacing. All echocardiographic studies were performed under stable hemodynamics and in sinus rhythm. Following the standards of our institutional hemodynamics protocol mean arterial blood pressure (MAP) and central venous pressure (CVP) were maintained establishing stable hemodynamics (MAP 60-80 mmHg, CVP 4-12 mmHg).

Surgical Management

Onpump CABG surgery was performed under normothermic conditions via median sternotomy. Full myocardial revascularization was achieved using single internal thoracic artery grafting and/or aortocoronary vein grafts, according to the clinical demands. After aortic cross-clamping cardiac arrest was achieved by blood cardioplegia. In all patients the pericardium was closed at the end of surgery.

Echocardiographic Assessment

We performed TEE after induction of anesthesia before sternotomy and any canulation of the patient. All measurements were done with Philips Epic 7 echocardiography machines and X8-2T-TEE probes. Examinations were performed by a board certified echocardiographer according to recent recommendations for TEE examination.[13, 14]

Real-time three-dimensional full-volume datasets, including the entire RV, were acquired from a mid-esophageal RV-focused four-chamber-view. Four-beat acquisition during apnea was performed. The settings of the ultrasound machine were adapted to a high temporal resolution. TomTec 4D-RV-Function-2.0 (TomTec Imaging Systems GmbH, Unterschleissheim, Germany) was used for estimation of three-dimensional derived RV-free-wall strain (3D-RV FWS) and RV ejection fraction (3D-RV EF). This software is based on speckle-tracking technology and provides a semi-automated quantification of RV size and function.[15, 16] Therefore, RV borders needs mandatory adjustment by the operator after automatic extraction and tracking of the right ventricle out of the full-volume data set.[16]Figure 1 shows the assessment of 3D-RV EF and 3D-RV FWS by TEE.

For the evaluation of tissue velocity of the tricuspid annulus (RV S'), tricuspid annular systolic excursion (TAPSE), and RV fraction area change (RV FAC) we used Philips QLAB 10.8 software. TAPSE was assessed in the midesophageal RV-focused four-chamber-view by measuring the displacement of the tricuspid annulus in anatomic M-mode. Anatomic M-mode is an angle independent M-mode that allows the operator to position the cursor freely on the two-dimensional image. Therefore, the cursor was directed towards the RV apex. RV FAC was evaluated from midesophageal RV-focused four-chamber view. The change of RV area in relation to diastolic RV area was calculated and is shown in percent. RV S' was assessed from the midesophageal RV-focused four-chamber view measuring the peak positive tissue velocity using pulsed wave tissue-Doppler imaging during ejection period in an angle-independent manner. Therefore, the cursor of the Doppler was directed towards the RV apex, which is available on all our Philips Epic 7 echocardiography machines. Settings of the ultrasound machine were adapted to high temporal resolution with a frame rate >100 frames/s. The sample volume of the pulsed-wave Doppler was set to 5-7 mm following recent suggestions of the European Association of Cardiovascular Imaging (EACVI).[17]

Outcome measures

We assessed the postoperative outcome measures of MACE (Major Adverse Cardiac Events as composite of stroke, cardiovascular death, instable angina pectoris, heart failure), stroke, transitory ischemic attack, shock, pneumonia, atrial fibrillation, renal replacement therapy, postoperative mechanical circulatory support, Redo CABG surgery or percutaneous revascularization. Moreover, we evaluated the duration of mechanical ventilation, duration of intensive care therapy, hospital stay and in-hospital death.

Statistical Methods

Statistical analyses of data were performed using MS Excel (Microsoft, Redmond, Washington), XLSTAT (Addinsoft, New York, New York) and the statistical software package R. Data was checked for normal distribution by visual assessment of histograms, Q-Q plots and additionally Shapiro-Wilk-test. Normally distributed data is presented as mean +- standard deviation, not normally distributed data as median with interquartile range (IQR). Percentiles were estimated using the function *quantile* of the statistical software package R with standard settings. Associations between 3D-RV FWS and patient outcomes was evaluated by linear (for continuous outcomes) or logistic (for binary outcomes) regression analysis. We adjusted for age and sex.

Results

3D-RV FWS analysis was feasible in 142 (95%) patients. All patients had a complete myocardial revascularization at the end of surgery and pericardial closure. None of the patients was pacemaker dependent or on inotropic or vasopressor support during echocardiographic evaluation. Baseline characteristics are presented in Table 1. Essential perioperative data are presented in Table 2.

No patient required intraoperatively inotropic or mechanical circulatory support after bypass, experienced shock or had a second run on CPB after termination of extracorporal circulation.

There were no postoperative complications in this patient population such as MACE, stroke, transitory ischemic attack, shock, pneumonia, or in-hospital death. No patient needed postoperatively renal replacement therapy, mechanical circulatory support, or redo CABG or percutaneous revascularization. Two patients (1.4%) had a ventilation time of more than 24 hours (34 and 39 hours, respectively) and ten patients (7.0%) developed atrial fibrillation postoperatively.

In our group of patients, median values with interquartile range (IQR) for 3D-RV FWS and 3D-RV EF were -25.2 (IQR -29.9 - -21.8) and 46.3% (IQR 41.0 - 50.1%), respectively. RV FAC, RV S' and TAPSE accounted for 39.7% (IQR 34.5 - 44.4%), 14.8cm/s (IQR 11.8 - 19.0cm/s) and 22 mm (IQR 20-25mm). There was no correlation of 3D-RV FWS and patient outcome, beside a small and clinically irrelevant correlation to prolonged in-hospital duration (r^2=0.03, p=0.02), in our group of patients. Normal values (2.5% to 97.5% percentile) for 3D-RV FWS and 3D-RV EF were -37.1 to -12.8 and for 34.9% to 58.2%, respectively, and amounted 24.6% to 52.1% for RV FAC, 5.7cm/s to 34.3cm/s for RV S‘ and 15.6mm to 31.5mm for TAPSE.

In 22 patients (15%) 3D-RV FWS was more impaired than -20, as suggested cut-off value for two-dimensional-derived (2D) RV FWS by recent guidelines on chamber quantification[5]. Considering only patients with 3D-RV EF [?]45%, regarded as *normal* for TTE-assessed 3D-RV EF by same guidelines,[5] we observed median values for 3D-RV FWS of -27.7 (IQR -31.5; -24.5) and a 2.5% to 97.5% - percentile of -38.5 to -17.1 in this subgroup of 86 patients.

Intraoperative values of 3D-RV FWS and the conventional echocardiographic parameters of RV function are presented in Table 3 and Figure 2 and 3.

Discussion

3D-RV FWS analysis is an innovative instrument for assessment of longitudinal RV function. In the present study we described intraoperativ *normal* values for 3D-RV FWS that can be expected in onpump CABG patient with preoperative preserved LV and RV function and an uneventful perioperative course, and compared them to conventional parameters of RV function assessment. Although, 3D-RV FWS assessment was already described as feasible, intraoperativ data are sparse.[11, 12, 18] Intraoperative evaluation RV strain and decision making is ambitious since there are no established reference values for anesthetized and ventilated cardiac surgery patients as there are for awake, spontaneously breathing patients in the non-operative setting.[5, 9] Therefore, our study has important findings.

In our group of CABG patients, with preserves LV and RV function and an uneventful intraoperative course we were able to measure 3D-RV FWS after induction of anesthesia, under stable hemodynamics, a predefined fluid management and without the influence of vasoactive support or pacing, in about 95% of our patients. These measured values for RV FWS are not *normal values* as it would be expected for healthy volunteers without cardiac disease, but *normal values* that can be expected in CABG patients with preserved LV and RV function, and a complication-free intraoperative course. In our opinion *normal values* from individuals without cardiac disease are not helpful in intraoperative decision making in cardiac surgery patients with different cardiac states (e.g., ischemia or subclinical myocardial dysfunction beside normal conventional parameters). Regarding existing literature, we are unaware of published reports on 3D-RV FWS in onpump CABG patients, beside our own pilot study.[12] Other authors report about 3D-RV FWS in different patient populations and clinical scenarios. Keller et al.[18] reported in a retrospective chart review about left-sided cardiac valve surgery patients with different grades of LV and RV function and different pulmonary pressure profiles. They described prebypass values of 3D-RV FWS of -19.4 +- 6 (95%-CI -20.9; -17.9) in 59 patients with normal pulmonary artery pressure profiles, but heterogenous LV function, and of -20.5 +- 7.3 (95%-CI -22.4; -18.6) in 60 patients with normal LV function, but different pulmonary pressure profiles. Patients in this group were treated with norepinephrine as clinical necessary. In another retrospective study Keller and colleagues[11] observed presternotomy TEE-assessed 3D-RV FWS values of -19.6 +- 6.9 in twenty-three off-pump CABG patients and -20.1 +- 7.1 in twenty mitral valve surgery patients, both groups again treated with vasoactive therapy as clinical necessary. In a huge retrospective study including 496 patients, Keller et al.[19] report about a heterogenous cardiac surgery patient population with different LV and RV function constellations including CABG and/or valve surgery procedure and even left ventricular assist device (LVAD) implantations in elective and urgent scenarios. Using a custom-made 3D mesh-derived software they were able to measure three-dimensional RV FWS. In their report they present values of this 3D mesh-derived RV FWS of -17.7 +- 6.9, assessed after induction of anesthesia and before sternotomy by TEE. Their patient population was supported by vasopressors and/or inotropes as clinically necessary. The presented data for 3D-RV FWS of our study patients could be considered as *normal* because our patient collection was less heterogeneous than the above-mentioned studies, not supported by vasopressor and/or inotropes and had no serious perioperative complications. However, 3D-RV FWS in our study was more declined than the *normal* values of TTE-assessed 2D-RV FWS reported by ASE / EACVI guidelines on chamber quantification[5] of -29+-4.5, or normal values of 2D-RV FWS from World Alliance of Societies of Echocardiography Study[20] of -28.3+-4.3, or from a metanalysis from Fine et al.[9] of -27+-2, described for all ages and genders in healthy individuals. Although all of our patients were preoperatively evaluated having preserved RV function by conventional parameters, 3D-RV EF was reduced (<45%) in 56 patients. Therefore, we evaluated 3D-RV-FWS also in a subgroup of our patients with 3D-RV EF [?]45%.

Differences in the altered described *normal* values might be explained by the more declined RV function in heart valve surgery and mixed populations of the retrospective studies from Keller and colleagues compared to our relatively healthy CABG population with preserved LV and RV function and without more than mild heart valve disease and without elevated pulmonary pressure. Our data are comparable to observed values for 2D-RV FWS measured by TTE after induction of anesthesia in non-cardiac surgery patients without myocardial disease reported by Dalla[21] et al. (-26.5+-3.9). Prospective observations of 2D-RV FWS by Donauer et al.[22] and Gronlykke et al.,[23] each with 30 CABG patients included, revealed higher mean values, which means a more declined RV function, in their patient populations of -22+-4 and -19.9+-7.2, respectively. This may be explained by differences in used assessment technique, different vendors of echo machines and probes, or by initially more declined RV function beside stated normal or preserved RV function, as evaluated preoperatively by conventional echocardiographic parameters. Our own pilot trial[12] showed a median 3D-RV FWS of -24.35 with an interquartile range (IQR) of -29.8 to -20.6. The fact that we measured RV function under stable hemodynamic conditions after induction of anesthesia, without influence of vasopressors or any other intravenous vasoactive therapy and in the absence of rhythm disorder may help to explain our data.

We have strengthened our trial in choosing a homogenous group of patients with preserved LV and RV function, homogenous procedures without influence of vasoactive support on echocardiographic evaluation, a predefined infusion regime and sinus rhythm, used only one vendor and type of echo machine and probes and used three-dimensional full-volume multi-beat acquisition that captures all essential structures through the entire cardiac cycle.

Our study has limitations. It is a single-center observational study including 150 patients. Evaluation of 3D-RV FWS is an "offline" analysis and mostly not incorporated in the echo machines at the moment. However, we suppose that this novel parameter will be included on the echo machines in the near future and become available for intraoperative "online" evaluation. We did not analyze regional differences of 3D-RV

FWS and did not evaluate for a correlation with localization of coronary heart disease. But most of our patients had triple vessel disease. Most of our patients were men older than 60 years, which might influence generalization of the results. Finally, we did not evaluate intra- or interobserver variability. Since our trial is a prospective single center observational study, the results need to be confirmed in further well-designed multicenter trials. Our data might help in to find reference values for intraoperative decision making in on-pump CABG surgery patients and could serve as a basis for further research.

Conclusion

We report *normal* values for intraoperative 3D-RV FWS considering a relatively healthy group of onpump CABG patients with an uneventful perioperative course, without the influence of vasoactive therapy or pacing, and without serious complications. Our data demonstrate that TEE-assessed values in anesthetized, and ventilated CABG surgery patients differ compared to reported TTE-assessed values in healthy, awake and spontaneously breathing patients without cardiac disease, but not the large extent as suspected in view of the mixture of procedures and heterogeneity of patient populations considered in other perioperative trials.

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